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LETTERS TO THE EDITOR

Cross-Talk Between Primary Percutaneous Coronary Intervention, Arterial Inflammation, and Light/Dark Patterns

We read with great interest the recent article by Glaser et al. (1). The authors should be congratulated for this well-conducted study. However, we would like to point out an important aspect in the interpretation of these findings.

Recent research has shown that inflammation plays a key role in coronary artery disease and other manifestations of atherosclerosis. Immune cells dominate early atherosclerotic lesions, their effector molecules accelerate progression of the lesions, and activation of inflammation can elicit acute coronary syndromes (2). The implication or association of physiological rhythms with peak activity at a certain time of day or night may be suspected, given that the onset of cardiovascular accidents follows a circadian pattern (3). Likewise, we have previously reported that in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention, day/night rhythms of inflammatory markers may be abnormal (4–6). A reciprocal link exists between inflammation and thrombosis. A better understanding of arterial inflammation will enhance our ability to prognosticate risk and effectively design therapy. Therefore, the presence of variability during the 24 h of inflammatory and immunologic functions, would, hypothetically, have a profound effect on the practice of primary percutaneous coronary intervention.

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Reply

I thank Dr. Dominguez-Rodriguez and colleagues for their interest in our paper (1) and appreciate the additional insight provided in their letter regarding the potential role of inflammation, and its diurnal patterns, in the differences in outcomes observed in patients undergoing primary percutaneous coronary intervention (PCI) during off hours versus routine hours. We agree that the role of inflammation and risk for plaque rupture and adverse short-term cardiovascular outcomes has become increasingly clear. In fact, in a prior report (2), we found that presentation with acute coronary syndrome as an indication for PCI was a potent independent risk factor for new lesion progression during the subsequent year; this finding further supports the role of inflammation, particularly in acute coronary syndrome patients.

In the present study (1), operators were more likely to state that a lesion did not respond appropriately during off hours when procedural success was not achieved. Although lesion characteristics by angiography were similar in both groups, flow characteristics were less favorable before PCI during off hours. Changes in inflammatory factors could certainly contribute to this finding, though phenomena such as platelet aggregation and activity changes with time have been previously described (3,4). In this regard, a study of blood markers of inflammation during off hours versus routine hours may prove valuable in establishing a link between inflammation and differential outcomes during off hours.

The possible role of inflammation highlights again our findings that multiple factors may be associated with poorer outcomes during off-hours PCI, including possible operator fatigue, a potentially modifiable risk factor. As health care policy is shaped, it is the understanding of other potential factors beyond door-to-balloon time, both institutional and biologic, that may ultimately improve outcomes in myocardial infarction.

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Intracardiac Echocardiography for Patent Foramen Ovale Closure: Justification of Routine Use

We read with interest the report by Hildick-Smith (1) and the accompanying editorial comment (2) in *JACC: Cardiovascular Interventions*. Dr. Meier (2) discussed the arguments for and against the use of ultrasound guidance during patent foramen ovale (PFO) closure. We wish to add further reasons to support the routine use of intracardiac echocardiography (ICE).

- ICE is ideal for evaluating the inferior interatrial septum and inferior vena cava rim—a region hard to fully assess with transesophageal echocardiography—to exclude additional shunts. A comprehensive study can be performed while the PFO closure device is being prepared and will not add to the procedure time.
- ICE requires experience, and limiting its use to only those PFO cases that are difficult or unusual restricts training and may therefore hamper interpretation of unusual anatomy.
- ICE can readily identify thrombus formation on the delivery sheath that can occur despite the use of full heparinization (3) and prevent procedural-related embolic events
- ICE assessment of the device and its relation to both the primum and secundum septum before final release is useful to confirm a stable position and adequate capture of the surrounding septum, as well as the alignment of the device with the aortic root and anterior mitral valve leaflet
- ICE reduces the fluoroscopy requirements, and in experienced hands, the majority of the procedure can be performed under ultrasound guidance only. This is useful in the rare cases of PFO closure being required during pregnancy.

We agree that ICE guidance during PFO closure usually necessitates a second operator experienced in intracardiac ultrasound. However, we disagree that introduction is a "fairly rough act" with a doubling in the risk of puncture site complications: the use of a long 11-F sheath and gentle passage of the probe along the inferior vena cava minimizes the risk of trauma with a 0% complication rate in a review of 155 cases of ICE-guided closure of atrial septal defect and PFO (4). It is possible that these complications are more likely to occur when operators use ICE infrequently.

We believe the routine use of ICE for PFO closure facilitates anatomical assessment and choice of closure device, reduces procedural complications with minimal additional risk, and ensures operators are sufficiently skilled to use ICE safely when a difficult PFO is encountered. These advantages offset the additional cost of the disposable probe.

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Reply

I thank Dr. Newton and colleagues for their interest in the paper of Hildick-Smith et al. (1) and my commentary (2). Obviously, neither the paper nor my commentary have convinced Dr. Newton and colleagues. Their letter will be appreciated by colleagues looking for reasons to stick to their habits of using intracardiac echocardiography (ICE) guidance during closure of the patent foramen ovale (PFO).

The inferior rim of a PFO is invariably at least 3 cm long and never a problem. I agree that tiny atrial septal defects in the flimsy central part of the septum primum are detectable by ICE and not by fluoroscopy. Yet they are very easily overlooked even with ICE, and they lack clinical significance. Paradoxical embolism through such a defect is highly unlikely as they are way off the inflow current of the inferior vena cava.